Office Action Summary	Application No.	Applicant(s)	
	10/582,116	BROWNLEE, MICHAEL A.	
	Examiner	**Art Unit**	
	MARCELA M. CORDERO GARCIA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7,18,19,23,24,29-31,51-54,62 and 67-70* is/are pending in the application.

4a) Of the above claim(s) *67-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7,18,19,23,24,29-31,51-54 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20100614* .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The previous Office Action mailed on 3/24/2010 is vacated and replaced by the following Office Action in order to correct for an error in the citation of a reference in the first 103 rejection. Examiner thanks Applicant's representative (Rebecca Eisenberg) for pointing this out in a telephonic conversation on 5/27/2010.

Election/Restrictions

1. Applicant's election without traverse of Group I, drawn to a method of inhibiting hyperglycemia-induced or free fatty acid-induced reactive oxygen formation comprising treating the cell with a pharmaceutically acceptable composition comprising GLP-1(9-36) in the reply filed on July 6, 2009 is acknowledged.

Applicant's election without traverse of the species corresponding to SEQ ID NO:1 and inhibition of hyperglycemia-induced reactive oxygen formation in the reply filed on July 6, 2009 is also acknowledged.

Status of the claims

2. Claims 1, 3, 4, 7, 18, 19, 23, 24, 29-31, 51-54, 62 and 67-70 are pending in the application. Upon searching the elected species Examiner found other species encompassed by the claims of Group I, which are herein examined for the sake of compact prosecution. Claims 67-70 are withdrawn as not drawn to the examined group/species. Claims 1, 3-4, 7, 18, 19, 23, 24, 29-31, 51-54 and 62 are presented for examination on the merits.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 51-54 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Coolidge et al. (US 6,429,197).

Coolidge et al. teach a method of administering to ischemia injured brain cells (e.g., in a human that suffered a stroke, cols. 2-3) a pharmaceutically acceptable composition comprising GLP-1(9-36) [e.g., cols 5-6, including SEQ ID NO:s 6 and 5 which are equivalent to instant SEQ ID NO:s 1-2] sufficient to control stroke-related hyperglycemia. (e.g., cols. 1-4). Coolidge et al. teach inhibiting hyperglycemia by administration of GLP-1(9-36) to a patient in need thereof such as a stroke patient (e.g., cols 1-8, claims). The methods include further administering a second active agent such as glucose or an oxygen radical scavenger (see claims 8-9 of Coolidge et al.). Coolidge et al. teach that the possible mechanism of glucose neurotoxicity remain speculative. Despite not knowing the precise mechanism, the fact is treatment with GLP-1 provides significant benefits. Importantly, and as a preventive of heightened damage and risk, GLP-1 can be and should be administered as soon as it is sensed that an event has, or is occurring. Thus it can be administered at home or in an ambulance for its immediate anabolic effect to improve brain metabolism. From these considerations it is clear that a potentially important strategy in treating acute stroke and in limiting infarct size is

controlling hyperglycemia, reducing blood glucose levels to the normo-or modest hypoglycemic range. And, until now, Coolidge et al. teach, the only practical means of treating hyperglycemia was with insulin. Administration of the GLP-1 analogs includes subcutaneous or micropressure injection, deep lung insufflation, external or implant pump, depot injection and other sustained release mechanisms, buccal and other cross skin and membrane mechanisms (e.g., claims 6-7, cols. 7-8). Please note that the limitation “inhibiting hyperglycemia-induced or free fatty acid-induced reactive oxygen formation in a mammalian cell" would be inherent to the administration to a human subject since it anticipates all the active steps of the instant invention as claimed (MPEP 2112). Further, Coolidge et al. teach that GLP-1 treatment after acute stroke or hemorrhage can be an ideal treatment because it provides a means for optimizing insulin secretion, increasing brain anabolism, enhancing insulin effectiveness by suppressing glucagon, and maintaining euglycemia or mild hypoglycemia with no risk of severe hypoglycemia. Further, Coolidge et al. teach that ischemia-induced membrane lipolysis, local acccumulation of membrane fatty acids and subsequent superoxide production during reperfusion-stimulated oxidation generates oxygen radicals that can damage neuronal membranes (i.e., nerve cells) by lipid peroxidation (e.g., col. 9), thereby teaching the limitation “sufficient to inhibit the free fatty acid-induced reactive oxygen formation”. With regards to the limitation “sufficient to inhibit the hyperglycemia-induced reactive oxygen formation in the cell" it is noted that Coolidge et al. teach bolus administration of 0.1 nmol/kg-75 nmol/kg and contiguous intravenous administration at 0.1 pmol/kg/min to 10 pmol/kg/min (e.g., col. 7). The instant application does not appear

to disclose what amounts are “sufficient to inhibit the hyperglycemia-induced reactive oxygen formation in the cell." Therefore, with respect to the art rejection above, please note that the Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether Applicants’ GLP-1(9-36) sufficient to inhibit the hyperglycemia-induced reactive oxygen formation in the cell (within the claimed method) differs and, if so, to what extent, from that of the discussed referen ce. Thus, with the showing of the reference, the burden of establishing non-anticipation by objective evidence is shifted to the Applicants.

Furthermore, “[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer.” Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. (See MPEP 2112).

Therefore the reference is deemed to anticipate the claims above.

5. Claims 1, 3-4, 7, 18, 19, 23, 29-30, 51-53 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al. (US 5,574,008, cited in the IDS dated August 13, 2009).

Johnson et al. (US 5,574,008) teach treating diabetes or hyperglycemia by administration of GLP- 1 (9-36) of, e.g., SEQ ID NO:s 1 and 2 (see claims 1-8 of Johnson et al.) to a mammal such as a human being (e.g., cols. 3 and 8, claims). Johnson et al. teach that the GLP-1 fragments have the ability to lower elevated levels of blood glucose in a mammal without stimulating insulin secretion (e.g., col.3). Johnson

et al. teach that the GLP-1 fragments may be administered intramuscularly and subcutaneously. Parenteral daily dosage preferably a single, daily dose are in the range from about 1 pg/kg to about 1,000 ug/kg of body weight, although lower or higher dosages may be administered. The required dosage will depend upon the severity of the condition of the patient and upon such criteria as the patient's height, weight, sex, age and medical history. Sustained release formulas may be achieved by the use of polymers to complex or absorb a compound. The controlled delivery may be exercised by selecting appropriate macromolecules. Johnson et al. do not expressly teach the limitation drawn to “inhibiting hyperglycemia-induced or free fatty acid induced reactive oxygen formation in a mammalian cell [...] sufficient to inhibit the hyperglycemia-induced or free fatty acid-induced reactive oxygen formation in the cell”. Please note that the limitation “inhibiting hyperglycemia-induced or free fatty acid-induced reactive oxygen formation in a mammalian cell" would be inherent to the administration to a human subject since it anticipates all the active steps of the instant invention as claimed (MPEP 2112). With regards to the limitation “sufficient to inhibit the hyperglycemia-induced reactive oxygen formation in the cell" it is noted that Johnson et al. teach parenteral daily dosage preferably a single, daily dose are in the range from about 1 pg/kg to about 1,000 ug/kg of body weight, although lower or higher dosages may be administered. The instant application does not appear to disclose what amounts are “sufficient to inhibit the hyperglycemia-induced reactive oxygen formation in the cell." Therefore, with respect to the art rejection above, please note that the Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether Applicants’

GLP-1(9-36) sufficient to inhibit the hyperglycemia-induced reactive oxygen formation in the cell (within the claimed method) differs and, if so, to what extent, from that of the discussed reference. Thus, with the showing of the reference, the burden of establishing non-anticipation by objective evidence is shifted to the Applicants.

Furthermore, "[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. (See MPEP 2112).

Therefore the reference is deemed to anticipate the claims above.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (US 5,574,008, cited in the IDS dated August 13, 2009) in view of Knudsen et al (US 6,268,343).

Johnson et al. are relied upon as above.

Johnson et al. do not expressly teach using a GLP 1(9-36) further having an additional Arg at the carboxy terminus.

Knudsen et al. teach GLP-1 analogs comprising GLP-1 (9-36) and having an additional arginine at the C-terminus, especially, e.g., Arg in position 38-39 (cols. 8 and 10) having a protracted profile of action relative and lower clearance. The analogs also were known to have insulinotropic activity, ability to decrease glucagon, ability to restore glucose competency to beta-cells and/or ability to suppress appetite/reduce weight (e.g., cols. 8-10). The pharmaceutical compositons may be administered parenterally, intramuscularly, subcutaneously, by an infusion pump, etc. in the treatment of diabetes mellitus (cols. 169-170).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Johnson et al. by using the analogs of Knudsen et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do so because Knudsen et al. taught that their analogs had a protracted profile of action and lower clearance than other analogs comprising GLP-1 (9-36) (e.g., col. 5). The analogs also were known to have insulinotropic activity, ability to decrease glucagon, ability to restore glucose competency to beta-cells and/ro ability to suppress appetite/reduce weight. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success since the GLP-1 analogs of Johnson et al. and Knudsen et al. were known to be effective in the treatment of diabetes mellitus and were also known to be administrable by similar ways, e.g., parenterally, intramuscularly, subcutaneously, etc.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed

invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

8. Claims 1, 3-4, 7, 18, 19, 23, 29-30, 51-53 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (US 5,574,008) in view of Vincent et al. (Ann. N. Y. Acad. Sci. 2002).

Johnson et al. is relied in detail as above. Johnson et al. teach a method of treating diabetes by administration of GLP 1 (9-36) of e.g., SEQ ID NO:s 1-2 (see claims). Johnson et al. do not expressly teach "inhibiting hyperglycemia induced reactive oxygen formation".

Vincent et al. teach that in hyperglycemia, the increased concentration of glucose rapidly induce production of reactive oxygen species in diabetic rats and that hyperglycemic conditions observed in diabetes mellitus are associated with oxidative stress-induced neuronal and Schwann cells death, and targeted therapies aimed at regulating ROS may prove effective in therapy of diabetic neuropathy (e.g., pages 374-381).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of Coolidge et al. to inhibit hyperglycemia and its functional effects such as hyperglycemia-induced reactive oxygen formation. One of ordinary skill in the art at the time the invention was made would have been motivated to do so because by reducing hyperglycemia, any dependent processes, such as formation of reactive oxygen species as taught by Vincent et al. (e.g., pages 374-381),

would also be reduced. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success since Johnson et al. was shown to reduce hyperglycemia (e.g., claims) in cases such as stroke, thus providing protection against ischemic damage.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

9. No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCELA M. CORDERO GARCIA whose telephone number is (571)272-2939. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marcela M Cordero Garcia/
Examiner, Art Unit 1654

MMCG 06/2010